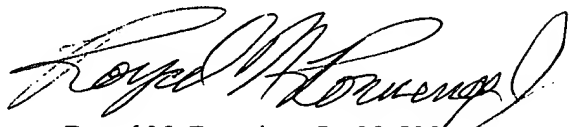
REMARKS

Claims 1-22 are pending in the instant application. Applicants have deleted claims 5, 7, 8, 9, 21, and 22 and have amended claims 1, 2, 3, 4, 6, 10, 11, 12, 13, 15, and 19 to more fully conform with U.S. practice and to delete multiple dependencies. A copy of the marked up claims showing the amendments, as well as a clean copy of the claims encompassing the amendments, is attached hereto.

Applicants respectfully assert that all amendments are fairly based on the specification, and respectfully request their entry.

Applicants believe that the claims, as amended, are in allowable form, and earnestly solicit the allowance of claims 1-20.

Respectfully submitted,



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Amended Claims (marked up copy showing amendment(s))

[Claims:]

What is Claimed is:

1. (amended) A method of generating a contrast enhanced image of a human or non-human animal subject which comprises administering to said subject an effective amount of a magnetic resonance imaging contrast agent and generating an image of at least part of said subject containing said agent, wherein said agent comprises a physiologically tolerable [lanthanide]Europium compound, preferably a chelate complex of Europium or a physiologically tolerable salt thereof having first and second oxidation states which [differ]differs in relaxivity by a factor of at least 5, and wherein said Europium compound is activated by switching between the II and III oxidation states of metal ions *in vivo* whereby contrast difference is enhanced in a body region in which conversion between the oxidation states occurs.[which is convertible *in vivo* from said first to said second oxidation state whereby contrast is enhanced in a body region in which conversion to said second state does or does not occur.]

2. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable [lanthanide]Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 10.

3. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable [lanthanide]Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 20.

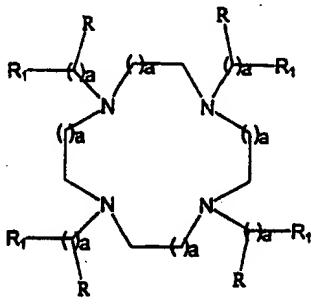
4. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable [lanthanide]Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 100.

6. (amended) A method as claimed in claim [5]1 wherein said change between two paramagnetic states is effected as a change from a spherically symmetric electronic ground state to a non-spherically symmetric excited state.[non-spherically symmetric electronic ground state to a spherically symmetric electronic ground state, or a change from a non-spherically symmetric electronic ground state to a spherically symmetric excited state.]

10. (amended) A method as claimed in [any one of claims 7 to 9]claim 1 wherein said chelate complex is a complex of a chelant selected from the group consisting of DTPA, EDTA, DTPA-BMA, DO3A, DOTA, HP-DO3A, TMT and DPDP.

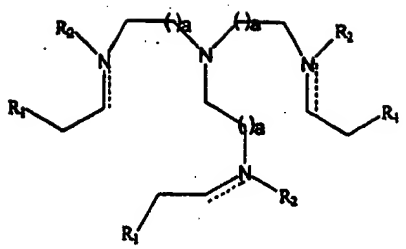
11. (amended) A method as claimed in [any one of claims 7 to 9]claim 1 wherein said chelate complex is a complex of a chelant selected from the group consisting of porphyrins and porphyrin-like molecules, phthalocyanines, crown ethers, hemin, heme, chelants having a square planar symmetry, cryptands and cryptates.

12. (amended) A method as claimed in [any one of claims 7 to 9]claim 1 wherein said chelate complex is a complex of a chelant selected from compounds of formulae (I), (II), (III), (IV), (V) and (VI):



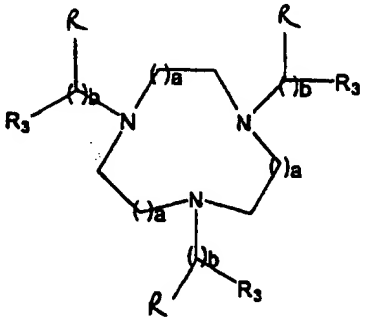
(I)

where each a independently represents an integer between 1 and 3, each R independently represents hydrogen or hydroxy and each R_1 independently represents a carboxylate, phosphate, thioacid, thiol, amino alkoxide or hydroxy group;



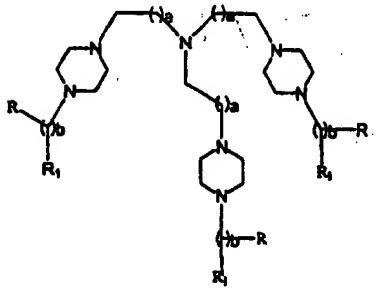
(II)

where a and R_1 are as hereinbefore defined and each R_2 independently represents hydrogen, C_{1-6} alkyl or aryl, with the proviso that R_2 is absent when the double bond is present on the same nitrogen;



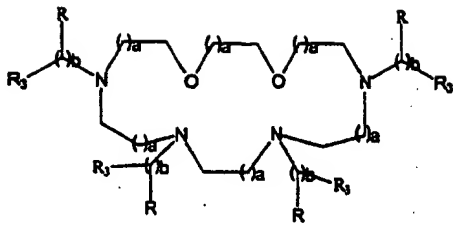
(III)

where a, R and R_2 are as hereinbefore defined, b is an integer between 0-3 and each R_3 independently represents R_1, $NR\text{-}NR_2\text{-}COO^{\theta}$, or $N{=}N\text{-}COO^{\theta}$ when b is positive or each R_3 independently represents $N{=}CH\text{-}COO^{\theta}$ or $NR_2\text{-}CH_2\text{-}COO^{\theta}$;



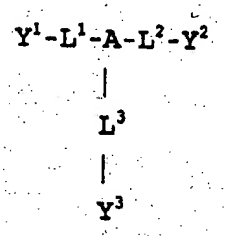
(IV)

where a, b, R and R_1 are as hereinbefore defined;



(V)

where a, b, R and R_3 are as hereinbefore defined;



(VI)

where A is N, CR_4, P, P=O, *cis,cis,cis*-1,3,5-trisubstituted-cyclohexane or an N,N',N"-trisubstituted-triaza 9 to 14 membered macrocyclic ring;

L^1,L^2,L^3 are linker groups which are independently chosen from C_{1-4} alkylene, C_{4-8} cycloalkylene or C_{4-8} o-arylene;

Y^1,Y^2,Y^3 are independently chosen from $-NH_2$, -B(=O)OZ, $-N=CR_5$-B(=O)OZ, $-NR_5$-CR_6-B(=O)OZ,-N[CR_6-B(=O)Q]$_2$ and –O-CR_6-B(=O)OZ where B is C or PR_6, each Q is independently –OZ or $-NR_6$, and Z is H or a counter-ion;

each R_4 and R_5 group is independently chosen from H, C_{1-5} alkyl, C_{1-5} lkoxyalkyl, C_{1-5} hydroxyalkyl, C_{1-5} aminoalkyl, C_{5-10} aryl or C_{1-6} fluoroalkyl;

R_6 is OH, C_{1-6} alkyl, C_{1-6} alkoxyalkyl, C_{1-6} fluoroalkyl, C_{1-10} alkoxy or C_{5-10} aryl;

with the proviso that at least one of Y^1, Y^2 and Y^3 is $-N=CR_5$-B(=O)OZ.

13. (amended) A method as claimed in [any preceding claim]claim 1 wherein said agent is conjugated to a biological vector capable of targeting said agent to a desired region of the body.

15. (amended) A method as claimed in [any preceding claim]claim 1 wherein conversion between said first and second oxidation states is effected *in vivo* by a localised

normal or abnormal biological process, by an administered chemical agent or by illumination of said agent with light.

19. (amended) An MR contrast agent composition comprising as an MR contrast agent a physiologically tolerable [lanthanide]Europium compound, preferably a chelate complex of Europium or a physiologically tolerable[or] salt thereof having first and second oxidation states which [differ]differs in relaxivity by a factor of at least 5, and wherein said Europium compound is activated by switching between the II and III oxidation states of the metal ions *in vivo*[which is convertible *in vivo* from said first to said second oxidation state] whereby contrast difference is enhanced in a body region in which conversion [to said second state does or does not occur]between the oxidation states occurs, together with an optionally encapsulated physiologically tolerable trigger substance capable of converting said contrast agent between said first and second oxidation states.